Reporting HCT/P Adverse Reactions

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Outline

- Background
- FDA Updates
 - MedWatch form
 - Guidance
 - Medsun program
- Summary of Received Reports
 - Pre- and Post- May 25
 - Tissue Safety Team

2005 New Reporting Requirements



FDA's Current Good Tissue Practices (21 CFR 1271)

HCT/P manufacturers

JCAHO Tissue Issuance and Storage Standards (PC.17.30)

For organizations that store or issue tissue (e.g.,hospitals)

FDA's Current Good Tissue Practice Reporting Requirement 21 CFR 1271.350

Manufacturers must investigate:

• **Any** adverse reaction involving a communicable disease related to an HCT/P that they made available for distribution.

Manufacturers must *report* to FDA

- An adverse reaction involving a communicable disease if it:
 - Is fatal
 - Is life-threatening
 - Results in permanent impairment of function or perm damage to body structure; or
 - Necessitates medical or surgical intervention, including hospitalization

FDA's Current Good Tissue Practice Reporting Requirement 21 CFR 1271.350

Adverse reaction means a noxious and unintended response to any HCT/P for which there is a reasonable possibility that the HCT/P caused the response.

To report adverse reactions to FDA, manufacturers must submit a MedWatch 3500A to FDA within 15 days of receipt of information

And provide follow-up information within 15 days of receipt.

JCAHO New Standards

PC.17.10, PC.17.20 and PC.17.30

PC.17.30 Investigate and Report Adverse Events

- Prompt reporting of adverse events from human cell and tissue transplants to the tissue establishment.
- Via phone, fax, mail or otherwise
- Not limited to communicable disease adverse events
- Can use MedWatch form to submit tissue or cell establishment and will assist with fulfilling JCAHO requirement for reporting.

http://www.jcrinc.com/subscribers/perspectives.asp?durki=9160&site =10&return=6065

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HCT/Ps on the Web

- Tissue Webpage:
 - www.fda.gov/cber/tiss.htm
- Webpage for Adverse Reaction Reporting:
 - www.fda.gov/cber/tissue/hctadverse.htm
- Guidance:
 - http://www.fda.gov/cber/gdlns/advhctp.htm

Updated MedWatch Forms

- New forms, effective 11/1/05:
 - Form FDA 3500 (voluntary)
 - Form FDA 3500A (mandatory) forms
 - Manufacturers may use old forms until 11/01/06
- Obtain forms at: www.fda.gov/medwatch/getforms.htm

Form FDA 3500A: Changes relevant to HCT/Ps

- "Suspect Medication" to "Suspect Product"
 - ⇒ Use Section **C** for HCT/Ps, not Section D (Medical Device)
- Addition of "Unique ID"
 - Use for HCT/P unique identification number

C. SUSPECT PROD	C. SUSPECT PRODUCT(S)						
Name (Give labeled stren	gih & minlaboler)						
#1							
42							
2. Dose, Frequency & Rou	te Used	3. Therap	py Dates (If unknown, gle) (or best estimate)	e distribuj			
#1		#1					
42		42					
4. Diagnosis for Use (India	ntionj		5. Event Absted After				
41			Stopped or Dose Re	☐ Doesnit			
42			91 106 NO	Apply			
6. Lot # 7. Exp. Date			#2 Yes No	□ Doesn't Apply			
#1	#1		8. Event Reappeared A Reintroduction?	Mor			
42	42		#1 Tyes TiNo	Doesnit			
9. NDC# or <mark>Unique ID</mark>			1———	☐ Apply ☐ Doesn't			
			A2 Yes No Apply				
10. Concomitant Medical P	roducts and The	rapy Dates	(Exclude treatment of ev	ent)			
D. SUSPECT MEDIC	CAL DEVICE						
1. Brand Name							
2. Common Device Name							
3. Manufacturer Name, City and State							
4. Model #	Lot #		5. Operator o	of Device			
Catalog #	Explication	Expiration Date (mm/dt/yyyy)					
Salaroy v	Exprission	- Louis process	□ Lay Use	r/Patient			

FDA Guidance on Adverse Reaction Reporting

- For "361" HCT/Ps
- Q/A format on adverse reaction reporting
- Provides guidance on filling out Form FDA 3500A Main points on form completion:
 - Complete Sections A, B, C, E and G
 - Section C:
 - Naming of Suspect Product: Use common name, followed by "(Tissue)" or "(Cell)" and then proprietary name.
 - Ex: Achilles Tendon (Tissue), JointSave
 - Provide Unique ID of HCT/P

Guidance: http://www.fda.gov/cber/gdlns/advhctp.htm

FDA Guidance on Adverse Reaction Reporting

Section G.

- Check off if "Initial Report" or "Follow-up"
- Manufacturer report number (Mfr Report #)
 - Use 10 digit FDA Establishment Identifier, year of report and sequential # for reports
 - Ex: 1234567890-2006-00005 (Use same # for follow-up reports.)
 - Mfr Report # also goes on 1st page of form

Adverse Reaction Reporting

- Don't forget 15-day follow-up when you have or receive additional information.
 - Follow-up reports should have same manufacturer # as initial rpt
- A tip:
 - Provide information on your internal investigation
 - Absence of processing deviations
 - Donor serology tests
 - Pre- and post- processing culture results
 - Complaints on same donor or lot
 - Other complaints of same pathogen
- May preclude follow-up phone call by FDA requesting more manufacturer information!

MedSun Tissue Pilot Project

MedSun is:

- A device surveillance program at ~300 hospitals
- Sponsored by FDA's
 Centers for Devices and
 Radiologic Health (CDRH)

Tissue Pilot Project is:

- Collaborative project with CDRH
- 28 participating hospitals (as of 1/19/2006)

MedSun functions:

- Internet based reporting; uses FDA 3500A
- Provides reports to mfrs and FDA quickly (same or next day)
- Assists hospitals with fulfilling JCAHO requirement
- Assists manufacturers with FDA reporting
 - Utilizes MedWatch 3500A form
 - Provides supplemental info
 - Mfr should include additional follow-up information to FDA

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Summary of MedWatch Reports:

Pre and Post May 25 (includes 361" and "351" products)

5/25/2005

6 months before	6 months after		
	% Increase		
55 reports	90 reports 64%		
Tissues: 22	Tissue: 55 150%		
Cells: 33	Cells: 35 6%		
Manufacturer: 25	Manufacturer: 35 40%		
Other: 30	Other: 55 83%		

Summary of MedWatch Reports: 2005 Reports by Product Type

	Total No.	Percent(%)
TISSUES	n=81	56.6
Bone	30	37.0
Skin	16	19.8
Eye	13	16.0
Cardiac Tissue/Blood Vessel	9	11.1
Musculoskeletal soft tissue	8	9.9
Bone and Tendon	3	3.7
Tissues, NOS	2	2.5
CELLS	n=62	43.4
Hematopoetic Progenitor Cells	52	83.9
Immune Cells	10	16.1
Total	n=143	100

Summary of MedWatch Reports: 2005 Reports by Event

	Number of Reports (Percent)		
	Tissues	Cells	Total
	n=81	n=62	n=143
Non-infectious adverse event	22 (27.2)	<u>41 (66.1)</u>	63 (44.1)
Infection	32 (39.5)	13 (21.0)	45 (31.5)
Product problem	8 (9.9)	7 (11.3)	15 (10.5)
Recall	15 (18.5)	-	15 (10.5)
Positive pre-implant culture	4 (4.9)	1 (1.6)	5 (3.5)

Summary of MedWatch Reports: 2005 Reports by Reporter

	Number of Reports (Percent)		
	Tissues	Cells	Total
	n=81	n=62	n=143
HCT/P manufacturer	22 (27.2)	<u>41 (66.1)</u>	63 (44.4)
Other (direct)	<u>59 (72.8)</u>	21 (33.9)	79 (55.6)
Medsun (% of Other) (nTissues=59, nTotal=79)	9 (15.3)	-	9 (11.4)

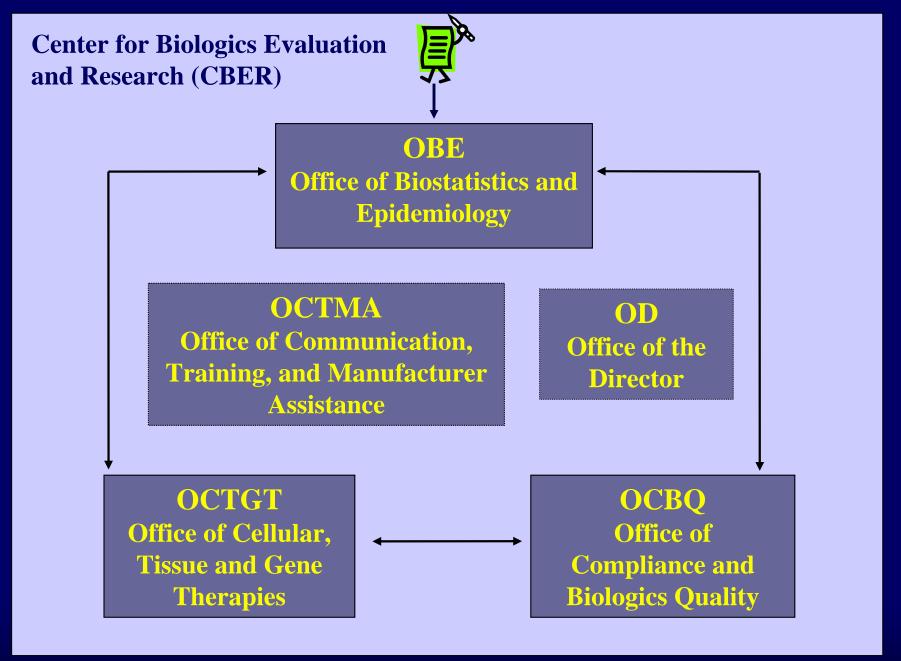
Summary of MedWatch Reports: CBER's Tissue Safety Team (TST)

Follow-up occurs if report:

"indicates an infectious disease transmission or possible transmission that may be associated with a 361 HCT/P" SOPP 8508

Involves gathering information from reporter or manufacturer, as indicated.

FDA's Tissue Safety Team (TST)



2005: TST Follow-up of Infection-Related Adverse Reactions

27 reports led to follow-up by TST

Bone: 8 Skin: 7

Eye: 6 Musculoskeletal Soft Tissue: 3

Cardiac/Blood Vessel: 2 Cells: 2

- Infections had serious outcomes: Explantation, additional procedures, prolonged antibiotics, retransplantation
- Majority showed no conclusive evidence of product being infected prior to transplantation
 - One case: 2 recipients of same donor's tissues developed infection with same pathogen

→ Voluntary recall already in effect; internal investigation found source of contamination

HIPAA and HCT/P Establishments 45 CFR 164.512(b)

- Permits covered entities to disclose protected health information (PHI), without authorization:
 - To non-public health authorities, if they are subject to FDA jurisdiction
 - For quality, safety or effectiveness of product regulated by the FDA
 - Examples of activities include:
 - Collecting or reporting adverse events
 - Tracking FDA-regulated products
 - Enabling product recalls or lookback (locating or notifying individuals who received recalled products)
 - Conducting post-marketing surveillance

Overall mission: Working together for HCT/P Safety



Questions on HCT/P adverse reaction reporting? Email tst@cber.fda.gov



